General Medicine 2014, vol. 15, no. 2, p. 126–135.

Original Article

Antiviral Face Masks for the Prevention of Influenza Infection: a Meta-analysis

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Objective: We performed a meta-analysis to examine the effectiveness of face masks for preventing influenza infection.

Methods: A literature search was conducted to identify clinical trials that compared the incidence of influenza infection among family members with and without the use of antiviral face masks; some trials also contained the use of hand hygiene in the intervention group. Data from each trial were combined using a random effects model with the DerSimonian-Laird method to calculate pooled odds ratios (ORs) and their corresponding 95% confidence intervals (CIs).

Results: The meta-analysis included seven randomized controlled trials that met our inclusion criteria. With the use of antiviral face masks, the pooled ORs (95% CIs) of laboratory proven infection were 0.69 (0.22–2.18). The pooled ORs (95% CIs) of influenza-like illness (ILI) were 1.07 (0.65–1.78). With the use of antiviral face masks and concomitant hand hygiene, the pooled ORs (95% CIs) of laboratory proven infection were 0.70 (0.35–1.39) in early intervention cases, and 0.93 (0.66–1.30) in all cases. The pooled ORs (95% CIs) of ILI were 1.01 (0.47–2.19) in early intervention cases, and 1.06 (0.53–2.13) in all cases.

Conclusion: No statistically significant differences were detected in the incidence of influenza infection by wearing antiviral face masks, suggesting that distribution of face masks in primary care settings may not be enough to prevent influenza-like illnesses amongst family members.

Keywords: face masks, influenza, prevention, meta-analysis

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Received for publication 22 August 2013 and accepted in revised form 30 October 2014

INTRODUCTION

Influenza virus infection is seen annually throughout the world. In Japan's winter season there is a high incidence and excess mortality from this infection, in addition to influenza-associated complications that occur particularly in infants e.g. influenza encephalopathy.[1] During the period of 9th March 2012 to 4th November 2013 inclusive, the estimated number of persons infected with influenza in Japan amounted to over 11 million.[2] The Japanese Ministry of Health and Labor suggested a number of methods for the prevention of influenza infection and its spread, including the following: 1) prophylactic vaccination, 2) self-covering of an infected person's mouth when coughing to prevent infection of other persons from airway droplet dispersal, 3) washing hands when coming back home, 4) maintaining adequate room humidity, 5) infected persons should take sufficient rest and intake of balanced nutrition, 6) infected persons should avoid crowds and visiting bustling and busy areas.[3]

As a countermeasure against infection through droplet dispersal of infection, the wearing of antiviral face masks is currently recommended; however, there is no clear evidence for the efficacy of this maneuver. A prior meta-analysis[4] supported the preventative measures against respiratory virus infection by the wearing of protective facial masks, gloves, and gowns as well as finger-hand hygiene. However, this was limited to a case-control study of contact with patients suffering with severe acute respiratory syndrome (SARS); in respect of the prevention of influenza infection, there has been no study to our knowledge looking at the use of antiviral facial masks with or without concomitant hand hygiene.

In a previous study examining the prevalence rate of respiratory infections through the wearing of surgical masks by individuals working in medical facilities, there was no effect for prevention of infection through this method.[5] In primary care, when influenza is diagnosed, there is a requirement to cope not only with the patients, but also their families who may become similarly affected. However, there has been no meta-analysis which has studied the preventative methods against influenza for the families of such patients. In this regard, we undertook a meta-analysis study to determine if secondary prevention could be achieved by instructing the use of antiviral face masks to families of infected patients with influenza.

METHODS

A) Acquisition of studies and the standard for inclusion

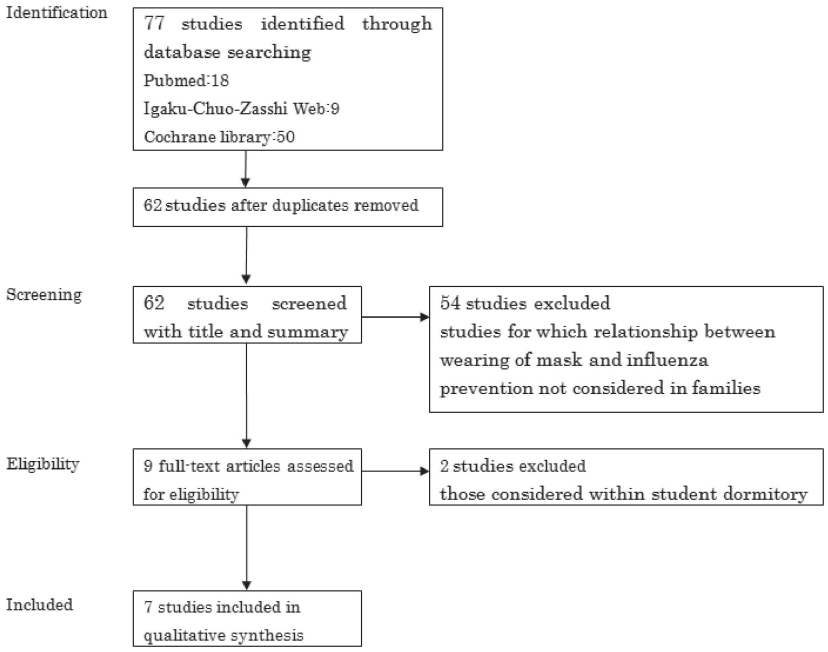
Appropriate studies we found by looking at the use of antiviral face masks among family members. We searched the PubMed, the Cochrane Library, and Igaku-Chuo-Zasshi (Japanese medical database) dating from 1980 to June 2012, inclusive. For the PubMed and the Cochrane Library, the following searchable keywords were utilized in various combinations including: mask, face mask, prevention, and influenza, and results were limited to English studies only. For the Igaku-Chuo-Zasshi Web, the following key words were searched including: mask, prevention, and influenza in Japanese. These search parameters were used in various combinations, and studies were identified by limiting them to comparative studies, randomized controlled trials, and quasi randomized controlled trials, respectively. Studies were selected that determined secondary infection of influenza in families of patients suffering with the infection and who were asked to wear antiviral face masks (face mask-wearing group) and those who were not asked to undertake this countermeasure (control group). We also looked at studies regarding individuals who worked at medical facilities. Those studies that did not examine secondary prevention of influenza infection were excluded.

The screening of selected studies was conducted from titles and summaries; all remaining studies, were examined in detail and were further considered for their inclusion eligibility. The search for studies and the consideration of their eligibility was carried out by several individuals and the results were compared to determine if the identified studies warranted inclusion for further analysis.

B) Extraction of data and evaluation of quality

The total number of persons affected by influenza from each study were identified for the intervention group and control group, respectively. With respect to the intervention study inclusion method, there were several

Figure 1. Flow chart for selection of study directed toward meta-analysis



reports with persons wearing face masks in addition to some studies also including the use of finger-hand hygiene. We considered that finger-hand hygiene could impact upon the study results quite apart from use of face masks, and hence this information was extracted and analyzed separately. For the evaluation of the quality of these initial studies the Jadad score was utilized.[6]

C) Statistical analysis

The control group was compared against the face mask-wearing group and mask-wearing and finger-hand hygiene combined group in respect of the onset of influenza. The pooled odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using the DerSimonian-Laird method with a random effect model.[7] Assessment of heterogeneity, was evaluated with value I^2 which is calculated as $I^2 = 100\% \times (Q - df)/Q$, where Q is Cochran's heterogeneity statistic which is the weighted sum of squares on a standardized scale and df the degrees of freedom.[7] There were two types of intervention groups in this meta-analysis, namely a face mask-wearing group and a face mask-wearing and finger-hand hygiene combined group, respectively. The included studies were assessed for the timing of onset of an intervention; those studies with onset of the intervention with 48 hours after onset of influenza (early intervention cases) and those studies with onset of anytime during follow-up (all cases). Influenza was assessed in several way including the use of the polymerase chain reaction (PCR) method on nasal and throat swab specimens, anti-influenza antibodies for index cases, and suspected clinical cases but not laboratory confirmed, which were referred to as influenza-like illness (ILI) cases. Finally, separate comparisons were undertaken with respect to the face mask-wearing group versus control group, the face mask-wearing and finger-hand hygiene combined group versus control group (early intervention cases and all cases). In total six meta-analyses were undertaken. Statistical analyses were conducted using Review Manager 5.2 (Cochrane Collaboration).[8]

RESULTS

A. Studies searched (Figure 1)

Sixty-two studies were identified after duplicates removed. Study titles and summaries were screened resulting in 54 studies being excluded with only nine studies remaining which met the inclusion criteria. A further two studies were excluded because the subjects were limited to residents of student dormitories and not

Table 1. Summary of studies (face mask-wearing group)

Study number	Author	Year	Country	Target persons	Intervention	Observation period	Outcome 1 Definition of test positive	Outcome 2 Definition of ILI	Outcome 1		Outcome 2		Jadad score (Randomization, Blinding, Withdrawal and Dropouts)
									Intervention	Control	Intervention	Control	
11	Benjamin J. Cowling et al	2008	China (Hong-Kong)	198 households 350 people of families who were diagnosed as outpatient rapid test positive or above 38°C	Distributed face masks	9 days	Visited on 3rd, 6th and 9th day after onset. Collected nasal and throat swab specimens from all. With virus culture or RT-PCR, influenza positive	CDC definition (fever of more than 37.8°C and sore throat)	4/61	12/205	5/61	8/205	3(2,0,1)
13	C. Raina MacIntyre et al	2009	Australia	145 households and 290 people of families of children (0–15 years old) who were positive for respiratory infection virus	Distributed face masks	7 days	Visited on day of onset of ILI and collected specimen and influenza positive with RT-PCR	Fever of more than 37.8°C, sore throat, coughing, sneezing, nasal secretion, nasal obstruction, one out of two types of headaches or diagnosed with test that either one is positive	1/94	0/100	19/94	16/100	3(2,0,1)
14	Laetitia Canini et al	2010	France	105 households and 306 people diagnosed as influenza and Quick view positive	Distributed face masks	7 days	—	Fever of more than 37.8°C or two or more of sore throat, coughing, nasal secretion, or fatigue	—	—	24/148	25/158	3(2,0,1)
15	Thorsten Suess. et al	2012	Germany	84 households and 218 people diagnosed with influenza and who were positive with qRT^PCR antigen test	Distributed face masks	8 days	Visited on 1st, 3rd, 4th, 6th, 8th day after onset. Throat swab collected from all, and with RT-PCR influenza positive	WHO definition (fever over 38°C, coughing and sore throat)	6/69 Within 36 hours 1/14	19/82 Within 36 hours 5/22	6/69 Within 36 hours 2/14	14/82 Within 36 hours 4/22	3(2,0,1)

ILI: influenza-like illness

Table 2. Summary of studies (face mask-wearing and finger-hand hygiene combined group)

Study number	Author	Year	Country	Target persons	Intervention	Observation period	Outcome 1 Definition of test positive	Outcome 2 Definition of ILI	Outcome 1		Outcome 2		Jadad score (Randomization, Blinding, Withdrawal and Dropouts)
									Intervention	Control	Intervention	Control	
12	Benjamin J. Cowling et al	2009	China (Hong-Kong)	Families 259 Households 794 people of patients diagnosed as influenza and with fever of over 38°C and outpatients rapid test positive	Distributed alcohol finger-hand sterilizer and face masks	7 days	Visited on 3rd and 6th day from onset. Collected from all nasal throat specimen, influenza positive with RT-PCR	CDC definition (fever of over 37.8°C, coughing and sore throat)	18/258 Within 36 hours 6/149	28/279 Within 36 hours 22/279	18/258 Within 36 hours 11/149	14/279 Within 36 hours 12/183	3(2,0,1)
16	Elaine L. Larson et al	2010	the U.S.	Families 509 Households 2788 Persons diagnosed as influenza were children below elementary school and who were Latino immigrants	Distributed alcohol finger-hand sterilizer and face masks	5 days	Visited on 1st and 2nd day after being diagnosed; collection of throat swab, quick diagnosis, and diagnosis as influenza with PCR, when occurring within 5 days among family members	CDC definition (fever of over 37.8°C, coughing, and sore throat)	25/938 Within 48 hours 25/938	24/904 Within 48 hours 24/904	79/938 Within 48 hours 79/938	105/904 Within 48 hours 105/904	2(1,0,1)
17	James M. Simmerman et al	2011	Thailand	885 people of families of influenza patients who were RT-PCR positive with antigen test	Distributed alcohol finger-hand sterilizer and face masks	21 days	Visited on 1st, 3rd, 7th day after onset. Throat swab and blood serum for RT-PCR day 1 and day 21 collected from all, and diagnosed as influenza with HI test	fever over 38°C and one of nasal secretion, nasal obstruction, coughing, conjunctival inflammation, frequent respiration, tachypnea, retractive breathing, sore throat, new convulsion	66/291 Within 48 hours 51/191	58/302 Within 48 hours 45/195	51/291 Within 48 hours 36/191	26/302 Within 48 hours 18/195	3(2,0,1)
15	Thorsten Suess et al	2012	Germany	218 people of 84 households of families diagnosed as influenza with RT-PCR positive	Distributed alcohol finger-hand sterilizer and face masks	8 days	On 1st, 3rd, 4th, 6th, and 8th day after onset. Throat swab and with RT-PCR influenza positive collected from all	WHO definition (fever of over 38°C and coughing, or sore throat)	10/67 Within 36 hours 1/24	19/82 Within 36 hours 5/22	6/67 Within 36 hours 1/24	14/82 Within 36 hours 4/22	3(2,0,1)

ILI: influenza-like illness HI test: Hemagglutination inhibition test

Figure 2. Funnel plot regarding comparison between face mask-wearing group and control group
OR: odds ratio
SE: standard error

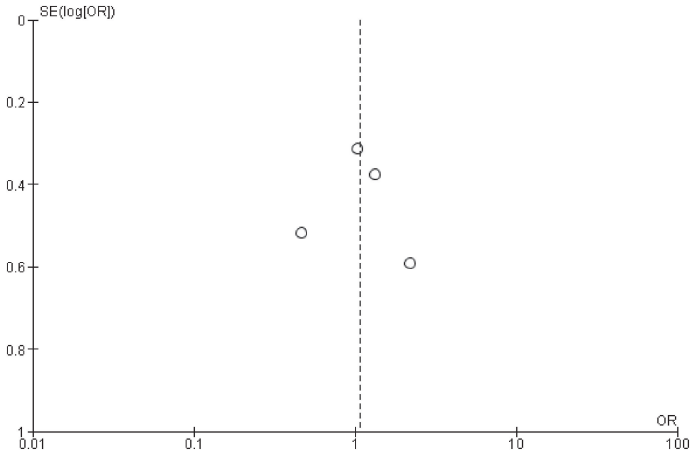
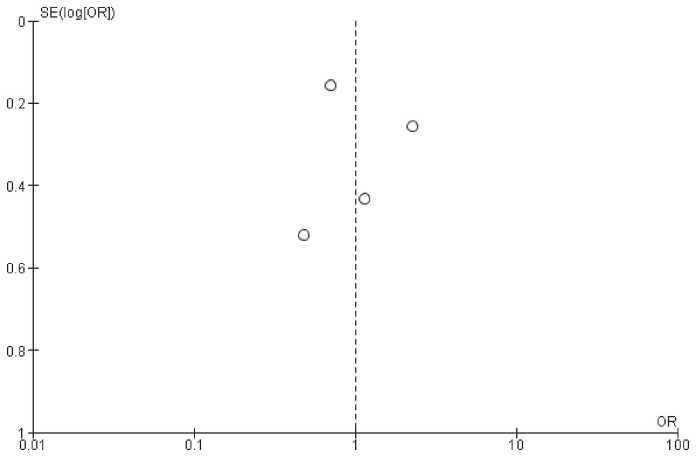


Figure 3. Funnel plot regarding comparison between face mask-wearing and finger-hand hygiene combined group and control group
OR: odds ratio
SE: standard error



families.[9,10] Finally, seven studies were analyzed which met the criteria for eligibility.

B. Overview of study (Table 1, 2, Figure 2, 3)

Of the seven studies analyzed, 67 persons were infected with influenza between 2008 and 2012. By country, there were two studies from China[11,12] and one from Australia,[13] France,[14] Germany,[15] the U.S.,[16] and Thailand,[17] respectively. All studies included all families that consisted of at least two members except the study of the U.S. that targeted only households with elementary school children. The purpose for the intervention was to give instructions to the families of patient's with influenza for prevention by distributing protective antiviral face masks and training in finger-hand hygiene by using sterilizing disinfectant. There were only four studies in which there was face mask use, and four studies that instructed the wearing of face masks along with finger-hand hygiene, with one case having both methods implemented. A comparison was made against controls, consisting of families given no advice with a patient suffering from influenza. The timing of intervention was determined at either 36 or 48 hours, with only one study defining the use of face

Figure 4. Meta-analysis with test positive as indicator among all those wearing face masks
IV: inverse variance
CI: confidence interval

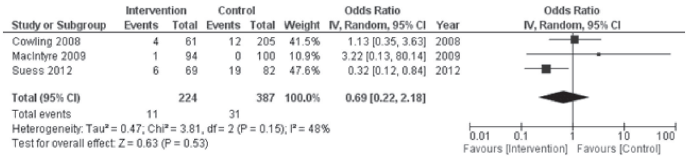


Figure 5. Meta-analysis with ILI as indicator among all those wearing face masks
IV: inverse variance
CI: confidence interval
ILI: influenza-like illness

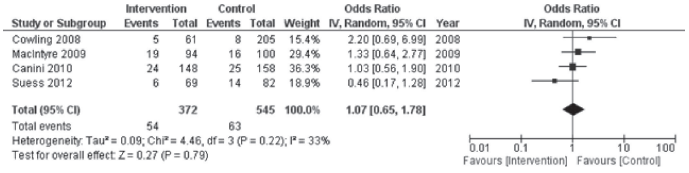
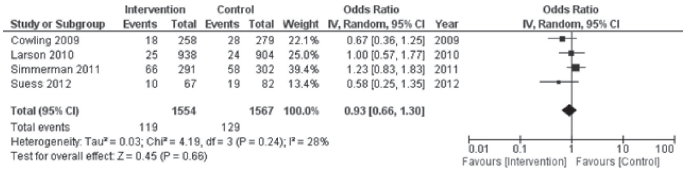


Figure 6. Meta-analysis with test positive as indicator for all cases of those both wearing face masks and using finger-hand hygiene
IV: inverse variance
CI: confidence interval



masks and four studies examining the use of face mask use with combined finger-hand hygiene, respectively. The observation period was more than five days, but serum influenza testing was also carried out 21 days later.[10] PCR and rapid testing of nasal and throat swab specimens were used to identify patients with influenza. ILI was diagnosed in patients with suspected influenza but without laboratory confirmation, by using the definitions of the World Health Organization,[9] the Centers for Disease Control[7,8] and a highly sensitive definition[10,12] from researchers. As a result of the evaluation of the quality of research using the Jadad score for randomization, withdrawal, and dropout, many studies showed good outcomes, but there was an absence of blinding in all of the studies. **Figure 2.3** shows a funnel plot which indicates that apparent publication bias was not observed.

C. Meta-analysis (Figures 4–9)

With regard to the face mask-wearing group alone with a family member who tested positive for influenza, the OR (95%CI) was 0.69 (0.22–2.18), whereas for ILI the OR (95%CI) was 1.07 (0.65–1.78). For the face mask-wearing and finger-hand hygiene combined group with a family member who tested positive for influenza, for all cases the OR (95%CI) was 0.93 (0.66–1.30), and in early intervention cases that was 0.70 (0.35–1.39). The ILI among all cases had an OR (95%CI) of 1.06 (0.53–

Figure 7. Meta-analysis with test positive as indicator of early intervention cases of both wearing face masks and using finger-hand hygiene
IV: inverse variance
CI: confidence interval

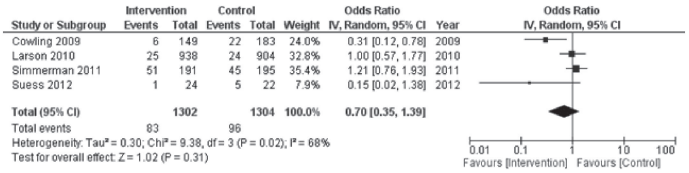


Figure 8. Meta-analysis with ILI as indicator of all cases of both wearing face masks and using finger-hand hygiene
IV: inverse variance
CI: confidence interval
ILI: influenza-like illness

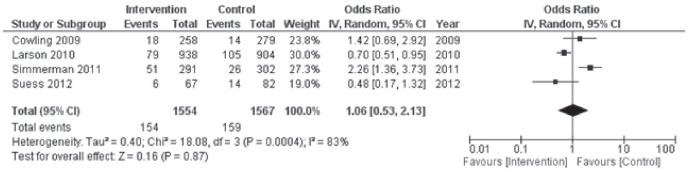
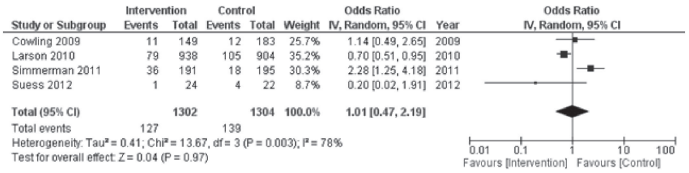


Figure 9. Meta-analysis with ILI as indicator of early intervention cases of those wearing face masks and using finger-hand hygiene
IV: inverse variance
CI: confidence interval
ILI: influenza-like illness



2.13), and with early intervention cases that was 0.70 (0.35–1.39). For ILI among all cases, the OR (95%CI) was 1.06 (0.53–2.13), and for early intervention cases that was 1.01 (0.47–2.19). The I^2 investigation of heterogeneity, revealed that each was 48%, 33%, 28%, 68%, 83%, and 78%, respectively in order.

DISCUSSION

The results show that no significant difference was seen in the onset of influenza among the intervention group compared to the control group at the time of the initial examination. The results also show that there was no evidence in supporting the use of wearing face masks and use finger-hand hygiene for influenza patient families. For issues regarding the intervention method itself, there may have been the possibility of face mask reuse or that face masks were not used correctly. Moreover, since the intervention for families was conducted after the onset of influenza and thereby prompting a hospital visit, it may have been possible that there was interfamily infection within the influenza incubation period prior to visiting a hospital, meaning that some cases could not have been prevented. With respect to studies of the differences in influenza

prevention, it is essential that they be analyzed thoroughly to determine if countermeasures of proper face mask use and finger-hand hygiene were properly instructed and carried out.

This study has several limitations. There is a potential selection bias due to the use of selected databases including the PubMed, the Cochrane Library, and the Igaku-Chuo Zasshi, the latter which also has language bias for Japanese. Moreover, the test of homogeneity indicated high heterogeneity of I^2 (more than 50%) in three out of six meta-analyses. The age distribution of the patient's family, socioeconomic conditions and vaccination rates might produce heterogeneity. For example in the study of the U.S.,[16] the criteria included only households with elementary school children, and for other studies, although 15–30% of children participated, the studies differed and distinguishing the age category differed and was unclear. For evaluation, one needs to consider such heterogeneities. The number of cases of influenza occurring despite preventative measure, which is the objective of this study, is also an issue when considering the social environment, living customs, and the differences in vaccination conditions amongst different countries. This means that results in one country may not be necessarily transferable to another country and therefore, country-specific studies of countermeasures should be undertaken. Moreover, for the prevention of droplet infection and contact infection, there is evidence that gargling is effective.[18] As a result, for epidemic prevention of influenza, the wearing of masks combined with effective hand hygiene and gargling may enhance preventive results in future studies.

In this study, for the first examination of patients suffering from influenza by physicians, influenza prevention was considered from the standpoint of public health, but to consider the epidemic result of influenza, it can be postulated that infection can be prevented by the continuous wearing of masks either in health or illness respectively. From this standpoint, it can be thought of that the rate of occurrence of influenza should be studies among groups and control groups.

CONCLUSION

This meta-analysis study has shown that the routine use of antiviral face masks and finger-hand hygiene of family members with a patient suffering influenza infection does not appear to prevent influenza-like illnesses amongst family members. There is a need to conduct further well designed interventional studies for the prevention of influenza infection before initial examination at a hospital.

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